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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/735,608	12/12/2003	Marcel P. Bruchez	5100-0702.20	1956

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ROBINS & PASTERNAK
1731 EMBARCADERO ROAD
SUITE 230
PALO ALTO, CA 94303

EXAMINER	
DO, PENSEE T	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 06/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/735,608	BRUCHEZ ET AL.	
	Examiner	Art Unit	
	Pensee T. Do	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *17-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16 and 38-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-41* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/22/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

T.D

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-16, 38-41, drawn to a composition and kit comprising of nanoparticles associated with a polymer, classified in class 436, subclass 525.

II. Claims 17-23, drawn to a method of enhancing the transport of a semiconductor nanoparticle across a biological membrane, classified in class 435, subclass 4.

III. Claims 24-37, drawn to a method of identifying a cell, classified in class 435, subclass 7.21.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II; I and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the method of using the product as claimed can be practiced with another materially different product such as a fluorescent label such as a dye instead of a nanocrystal coupled to a polymer and a biological active agent.

Inventions II and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of

operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions the two groups are drawn to two different methods with different purpose and method steps, one is a method of enhancing the transport of a semiconductor nanoparticle across the biological membrane and the other method is to identify a cell. The method of enhancing the transport does not require a detection step. Thus, these two groups have different modes of operation, different functions and are not capable of use together.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

Because these inventions are distinct for the reasons given above and the search required for Group I is not required for Group II or III, restriction for examination purposes as indicated is proper.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

During a telephone conversation with Ms. Roberta Robins on June 22, 2005 a provisional election was made without traverse to prosecute the invention of group I, claims 1-16, 38-41. Affirmation of this election must be made by applicant in replying to this Office action. Claims 17-37 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-16, 38-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite for reciting "associated" in line 2 because it is unclear of how the nanoparticle is associated with a cationic polymer, is it bound to or in proximity to the polymer? See also claim 12 for the same problem.

Claim 1 is also indefinite for reciting "capable of" in line 2 because it is unclear of how the polymer is modified in order to be capable of enhancing the transport of the semiconductor nanoparticle across the membrane. See also claim 12 for the same problem.

Claims 38-41 are indefinite for reciting "instructions for preparing ***encoded cells***" because the composition of the claims 1, 12, 14 and 16 have nothing to do with encoding cells.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7, 10-13, 16, 38, 39, 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bawendi et al. (US 6,306,610) in view of Rothbard et al. (US 6,306,993).

Bawendi teaches a composition comprising fluorescent semiconductor nanocrystals associated to a molecule such as cells, prokaryotic or eukaryotic. The semiconductor nanocrystals comprise a CdSe core and a ZnS shell. The composition is also associated with cell membranes. (see col. 3, line 60-col. 4, line 62; col. 19, lines 58-60; col. 20, lines 51-59; col. 29, lines 41-42).

However, Bawendi fails to teach the nanoparticle is associated with a cationic polymer capable of enhancing the transport of the semiconductor nanoparticle across a biological membrane; wherein the cationic polymer has from 5 to 25 contiguous Lys and/or Arg residues. Bawendi also fails to teach a kit comprising a semiconductor nanoparticle complex according to claims 1, 12, 16 and instructions for preparing the encoded cells using the semiconductor nanoparticle complex. Bawendi also fails to teach the cationic polymer is a tat peptide from protein transduction domain of the HIV tat protein.

Rothbard teaches methods and composition for transporting drugs and macromolecules across biological membranes wherein the biological membranes are

contacted with a conjugate containing a biologically active agent that is covalently attached to a transport polymer. Such transport polymer has 6 to 25 subunits of L-Arginine. The transport enhancing polymers are exemplified by peptides in which arginine residues constitute the subunits. Exemplary eukaryotic cell membranes of interest include membranes of dendritic cells, epithelial cells, endothelial cells, keratinocytes, muscle cells, fungal cells, bacterial cells, plant cells and the like. Biological active agents are macromolecules such as nucleic acids, peptides, proteins and analogs thereof. The agent may be linked to the polymer by a linking moiety. The composition includes a conjugate containing a biological active agent covalently attached to at least one transport polymer and can be packaged with instructions for using it. (see col. 2, line 44-col. 4, line 45; col. 5, lines 47-58). The transport polymers contain short-length polymers from 6 to 25 subunits. The conjugate is effective to enhance the transport rate of the conjugate across the biological membrane relative to the transport rate of the non-conjugate biological agent alone. (see col. 6, line 63-col. 7, line 5). Detecting uptake of macromolecules may be facilitated by attaching a fluorescent tag. (see col. 11, lines 3-4). Fluorescently labeled peptide polymers composed of 6 or more arginine residues entered cells more efficiently than the tat sequence 49-57 in fig. 1 (see col. 11, lines 30-40). Since the polymer of Rothbard composes of 6 to 25 contiguous Arg residues, it must be a cationic polymer.

Since Bawendi and Rothbard both teach using a label such as nanocrystals for cells or cell membrane, it would have been obvious to one of ordinary skills in the art to associate the polymer, which comprises of 6 to 25 subunits of Arg residue, taught by

Rothbard to the nanocrystals as a fluorescent label and use in the composition of Bawendi because macromolecules such as peptides and oligonucleotides experience difficulty in passing across the biological membrane and having a polymer as that of Rothbard enhances trans-membrane transport. Furthermore, the nanocrystals of Bawendi can be used a label which associates with the polymer to so that measures of biological molecules transported across the biological membrane can be easily detected because the nanocrystals of Bawendi associates with the biological membrane.

Regarding claims 38, 39 and 41, it would have been obvious to one of ordinary skills in the art to package the combined composition taught by Bawendi and Rothbard with instruction for using it for economical convenience since Rothbard teaches packaging the polymer with biological active agent into a kit with instructions for using it.

Claims 8, 9, 14, 15 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bawendi et al. (US 6,306,610) in view of Frankel et al. (US 5,652, 152).

Bawendi has been discussed above.

However, Bawendi fails to teach that the cationic polymer is tat peptide from the protein transduction domain of the HIV tat protein and a kit comprising the composition of claim 14 with instruction of using. Bawendi also fails to teach the sequence ID NO. 1 comprising of Arg Lys Lys Arg Arg Gln Arg Arg Arg.

Frankel teaches intracellular delivery of cargo molecules by the use of transport polypeptides which comprise HIV tat protein or one or more portions thereof and which are covalently attached to the cargo molecules. The transport polypeptides are

characterized by the presence of the tat basic region (amino acids 49-57). The biological active cargo molecules such as polypeptides, nucleic acids are delivered/transported into the cytoplasm and nuclei of cells in vitro and in vivo. (see abstract). Label such as a fluorescent was used to study the transported molecules across the cell membrane. The label is attached to the tat peptide. (see col. 42, lines 24-29). Frankel teaches sequence ID No. 4, amino acids 12-20, comprising Arg Lys Lys Arg Arg Gln Arg Arg Arg. (see col. 55-56, sequence ID. NO. 4).

It would have been obvious to one of ordinary skills in the art to use the HIV tat peptide for transporting biological molecules across the cell membrane as taught by Frankel and attach it to a fluorescence semiconductor nanocrystal which associates to a cell membrane so that when biological molecules to be transported reach the cell membrane, they can be transported effectively and efficiently with the aid of the tat peptide and their activity or measurement can be detected by the nanocrystals since the nanocrystals have a spectral emission that is tunable to a desired wavelength, and wherein said wavelength provides information about a biological state or event. It would have been obvious to one of ordinary skills in the art to package the combined composition into a kit with instruction of using it for economic convenience since Frankel teaches that the tat polypeptide can be used as research laboratory reagents, either alone or as part of a transport polypeptide conjugation kit. (see col. 7, lines 30-32).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 7:00-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Pensee T. Do
Patent Examiner
June 24, 2005

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

06/24/05